

WHAT IS CLAIMED IS:

1. A method for rapid haplotyping comprising the steps of:

labeling at least two target sites on a segment of DNA or RNA with separate distinguishable luminescent hybridization probes, where the targets are selected genetic markers; and

5 detecting the presence or absence of each luminescent hybridization probe on each DNA segment to determine the haplotype of each DNA or RNA segment.

2. A method for rapid haplotyping comprising the steps of:

labeling at least two target sites on a segment of DNA or RNA with separate distinguishable luminescent hybridization probes, where the targets are selected genetic markers;

5 forming a dilute solution containing the labeled DNA or RNA segments; illuminating each labeled DNA or RNA segment with light beams; and detecting the presence or absence of each luminescent hybridization probe on each DNA segment to determine the haplotype of each DNA or RNA segment.

3. The method of Claim 1, further including the step of sequentially and repeatedly haplotyping pairs of neighboring genetic makers on DNA segments forming a chromosome.

4. The method of Claim 1, wherein the step of detecting the presence or absence of each luminescent hybridization probe includes the step of detecting a luminescence characteristic emitted from each hybridization probe and cross-correlating the detected luminescence characteristic to indicate the presence or
5 absence of both hybridization probes on a single DNA or RNA segment.

5. The method of Claim 2, wherein the step of detecting the presence or absence of each luminescent hybridization probe includes flowing the dilute solution of the DNA or RNA through a flow cytometer.

6. The method of Claim 2, wherein the step of detecting the presence or absence of each luminescent hybridization probe includes examining individual drops of the solution containing DNA or RNA with a confocal microscope.

7. The method of Claim 6, wherein the step of examining individual drops of the solution with a confocal microscope includes scanning each drop through a stationary probe volume or scanning the probe volume through a stationary drop.

8. The method of Claim 1, 2, 3, 4, 5, 6, or 7, wherein the targets are base sequence variations selected from the group consisting of single nucleotide polymorphism, multibase deletion, multibase insertion, microsatellite repeats, dinucleotide repeats, tri-nucleotide repeats, sequence rearrangements, and chimeric sequence.

9. The method of Claim 1, 2, 3, 4, 5, 6, or 7, wherein the luminescent hybridization probes are selected to have distinguishable characteristics selected from the group consisting of luminescence emission spectral distribution, lifetime, intensity, burst duration, and polarization anisotropy.

10. The method of Claim 9, wherein the luminescent hybridization probes are formed from the group consisting of single dye molecules, energy transfer dye pairs, nano-particles, luminescent nano-crystals, intercalating dyes, and molecular beacons.

11. The method of Claim 9, wherein the form of the hybridization probe is selected from the group consisting of DNA, RNA, PNA, and LNA.

12. The method of Claim 8, wherein the luminescent hybridization probes are selected to have distinguishable characteristics selected from the group consisting of luminescence emission spectral distribution, lifetime, intensity, burst duration, and polarization anisotropy.

13. The method of Claim 12, wherein the luminescent hybridization probes are formed from the group consisting of single dye molecules, energy transfer dye pairs, nano-particles, luminescent nano-crystals, intercalating dyes, and molecular beacons.

14. The method of Claim 12, wherein the form of the hybridization probe is selected from the group consisting of DNA, RNA, PNA, and LNA.

15. The method of Claim 1, 2, 3, 4, 5, 6, or 7, where the hybridization probes are selected from the group consisting of single probes that are specific for each target or multiple probes that act together to identify the target.

16. The method of Claim 15, wherein the single probes are selected from the group consisting of oligo DNA, oligo RNA, oligo beacon, oligo PNA, oligo LNA, and chimeric oligos.

17. The method of Claim 15, wherein the multiple probes are selected from the group consisting of hybridization pairs, invader oligo pairs, ligation oligo pairs, mismatch extension 5'-exonuclease oligo pairs, energy transfer oligo pairs, and 3'-exonuclease pairs.

18. The method of Claim 12, where the hybridization probes are selected from the group consisting of single probes that are specific for each target or two probes that act together to identify the target.

19. The method of Claim 18, wherein the single probes are selected from the group consisting of oligo DNA, oligo RNA, oligo beacon, oligo PNA, oligo LNA, and chimeric oligos.

20. The method of Claim 19, wherein the two probes are selected from the group consisting of hybridization pairs, invader oligo pairs, ligation oligo pairs, mismatch extension 5'-exonuclease oligo pairs, energy transfer oligo pairs, and 3'-exonuclease pairs.

21. The method of Claim 1, 3, or 4 including forming a dilute solution to a concentration in the range of 100 nM to sub-fM of DNA or RNA fragments.